Opinion Article

Model scientists

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There is an increasing trend for the focus of biology to be determined more by administrators who have short-term pecuniary interests in science rather than by individuals who are "doing science" to further the fundamental human desire to understand ourselves, the natural environment, and our place in the world, though questioning. We feel that this ceding of the scope of science from the questioners to the administrators is at variance with the traditions of science, which heretofore have resulted in the remarkable advancements made in the field of biology. In contrast to the plethora of day-to-day conversations on how to fit into the administrators' directives, this essay provides a historical context, particularly though its extensive bibliography, to encourage today's biologists to question authority and question nature.

"If it be of importance and of use to us to know the principles of the element we breathe, surely it is not of much less importance nor of much less use to comprehend the principles, and endeavour at the improvement of those laws, by which alone we breathe it in security."—Jeremy Bentham¹

"Science", according to Erwin Chargaff, "is the application of reason, and mainly of logic, to the study of the phenomena of nature. Therefore, the most important scientific tool is the human brain. Each brain sits in its own head. Hence, the all-important unit in research is the individual scientist." Indeed, Ernst Haeckel goes as far as saying, "The scientific results of an institute are in inverse proportion to its size." Given the importance of the individual scientist in doing science, it is ironic that we often see references to "model organisms" in published papers and job descriptions, yet it is rare to find the phrase "model scientist" in any context.

It is up to each individual to choose his or her own examples of model scientists. Moreover, we feel that each individual has a responsibility to choose and study such models, in part, because those models that have endured provide a standard of excellence against which any one of us can compare our own accomplishments (or lack thereof). At the beginning of each semester we ask our students to name who they think are the ten best scientists who ever lived. Then we ask if they have ever read any of their original works. In

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the majority of the cases, they have never read a single work by the people they consider to be the best scientists. This is a shame. They read the works of others, but not the works of the people who they consider to be the best. We encourage them to read the words of their own model scientists, and to take a journey through the minds of the scientists they admire.⁴⁻⁶

To us, model scientists are persons whose primary goal is to reveal the underlying laws of Nature. In order to do so, the Prometheans of biology search out the organisms (really taxon or taxa) or groups of organisms that have the morphological, physiological, biochemical, genetic or ecological features that allow them to answer the problem in question. Alternatively, when working on a given organism or group of organisms, a model scientist determines how this organism or taxon can best be studied to discover new biological principles. In order to assess what is new, one must know what is old. Thus, the model scientist must know the history of the field.⁷⁻¹⁰ The passion for seeking a broad generalization is often tempered by the realization that each search must be amenable to quantitative study. 11 Thus in order to do something that "is good in itself and has broad implications" the model scientist has the depth of knowledge and skill necessary to use the techniques that are best suited to answer the question. The model scientist understands the laws of physics and chemistry, which underlie the majority of the techniques used. In this way the model scientist understands the qualitative and quantitative relationships between the question and the answer, and is also in a position to refine old techniques or create new ones in order to further our understanding of the problem. Choosing the right technique often means that the scientist understands the power of numbers, and thus can relate the sensitivity of the technique to the order of magnitude of the process. The model scientist understands that every answer is a mixture of fact and hypothesis, and clearly delineates the difference and strives to increase the ratio of fact to hypothesis.³ The model scientist presents his or her work through publications and/or teaching. The model scientist understands the relationship between the scientific work and the society at large, and has the fundamental virtues of courage and integrity to deliberate and act upon any related ethical issues. 12-16 The model scientist has the courage to question authority, and looks at everything he or she does with skepticism and from first principles. 17-21 Below we will describe the intellectual history of model scientists.

At the dawn of our civilization, religion provided a forum where people could ask questions like "What is life? What is the nature of the world? What are the causes of the things we see? Where did we come from? And what is our relationship to the Universe?" By the

close of the Middle Ages it seems that some religious and academic authorities decided that they knew the answers to these questions, and it was blasphemous even to ask the questions. Following this decline in the leadership of religious institutions in providing an environment in which to understand the natural world through questioning, the new field of natural philosophy arose to provide a forum in which people could again ask these questions; and since the renaissance, natural philosophy has been remarkable in its ability to provide answers to such questions. Both theology and natural philosophy seek to understand the world through questioning, however natural philosophy has the advantage of opening up many more questions, since even if a natural philosopher believes that God is the first cause of every effect, there are still many important secondary causes to understand between any given cause and effect. We are afraid that we have entered a period when the questioning of science is hampered again by a new group of authorities—authorities with the power of Bishops and Popes—who are less interested in the questions posed to understand the relationship between cause and effect, than they are interested in the effect—and a certain effect at that—Is the process under study capable of garnering large amounts of money in the form of overhead, patent royalties and licensing agreements? These pecuniary questions have decided which scientific questions should be answered, and it has become blasphemous, or rather in today's parlance, "unfundable", "unhirable" or "untenurable" to ask other questions.^{22,23}

Certain organisms that have the advantage of having DNA sequences that are easily identified, isolated, patented and licensed are better suited for answering these pecuniary questions in the affirmative. These organisms have come to be known as "model organisms". The current concept of a "model organism" arose, in the main, at a time when some governments no longer felt obliged to support science in the manner they did during the cold war and in exchange, universities were allowed to make profits from patents. Other governments, working with limited budgets, followed suit to become more competitive on the world stage. Model organisms are used by the majority of scientists primarily because research on them is fundable and fashionable.^{24,25} It is our opinion that the first question asked by a biological scientist today is typically not "What is life?" but "Is it fundable?" We have entered the era of "sell buy-ology".

We are strong believers in independent thought, and do not like the idea of absolute authorities. ²⁶⁻³⁰ We believe, along with Isocrates, that power corrupts and absolute power corrupts absolutely. ³¹ Indeed, we hold that scientists must have freedom from authoritarianism in order to search for the truth where they believe it may be found. This freedom should only be limited by the ethical principles codified by the society in which the scientist lives. Science has progressed, to a large extent, through the actions of a limited number of individual and free scientists. ^{2,31-34} Examples where science has been hurt by the power of authority (through either totalitarianism or centralization) are given in the following references. ³⁵⁻⁴⁴

As humans emerging from the cave, we have tried to make sense of the world around us.⁴⁵ We made observations about the obvious features that affect us. We found that the Sun was warm and bright. We found that rubbing sticks together caused heat and fire. We found that eating the plants or animals around us, and drinking the water from the lakes and streams were necessary for sustaining life. As

we made more and more observations, and gathered more and more facts, we began to systematize the data, and make generalizations, like cereal grains, fruits and eggs were good to eat. As we acquired more and more data, and strung them together with more and more hypotheses, we could then make predictions. For example, the seeds available in a newly inhabited place looked very much like the seeds from the old place, and thus they would probably be good to eat. As our brains developed, we gained the ability to make more and greater generalizations.

In our day-to-day living, we observed that plants grew from seeds; an offspring looked like a mixture of his/her mother and father; stones fell from high places; streams flowed downhill; the Sun returned every day, and the moon appeared to follow a 28-day cycle. Realizing that in our everyday world, all effects were produced by causes, we looked for causes for everything. As with any new endeavor, sometimes the generalizations were reliable, sometimes not. Yet we were a questioning species, and religion provided the place to ask questions. The most scholarly answers for the causes of all these natural phenomena from vital processes to astronomical events, whether reproducible or catastrophic, were God(s). We felt comfort in knowing the relationship between the supernatural cause and the plethora of effects that surrounded us, and it was good.

Around the 6th and 5th centuries BC, a few philosophers scattered around the Ionian and Aegean Seas believed that the world was intelligible in terms of natural processes and/or mathematical descriptions as opposed to direct supernatural causes. Thales, Heraclitus, Pythagoras, Empedocles and others weaved their limited observations of Nature into grand theories of the world. 46-54 Perhaps Aristotle was the first model scientist. Aristotle, in the 4th century BC, in the democratic city of Athens, took observational evidence very seriously in order to understand the nature of the world. Unlike his teacher Plato, Aristotle believed that we could understand the world around us only by observing it. He was especially interested in observing animals in his search to understand the nature of the world because he felt that there was a very close connection between cause and effect in animals. Aristotle dissected chicken embryos and observed that the first sign of life was a tiny red speck, which he considered to be the heart; and concluded that the heart, more then any other organ, represents life itself.⁵⁵

Aristotle provided support for this observation by dissecting goats. He somehow got his hands on healthy goats, which were brought to a nearby temple to be sacrificed. He noticed that the healthy goats had healthy hearts, yet their other organs showed signs of decay. By contrast, he observed that goats that died of natural causes had diseased hearts. Thus Aristotle concluded that the life and death of an individual was related to the life and death of its heart.

In the 3rd century BC, physicians including Herophilus and Erasistratus, living in the Hellenistic City of Alexandria, furthered the anatomical studies begun by Aristotle by doing dissections on animals and man. According to Celsus, Herophilus and Erasistratus did vivisections on condemned criminals (which were the model organisms at the time). In the course of their dissections, Herophilus discovered the central nervous system, and Erasistratus discovered the arterial and venous systems.

In the 2nd century AD, following the conquering of the Hellenistic world by Rome, Galen, the imperial physician of Rome, continued to dissect animals with his own hands, in order to ensure the quality

of the dissections and the completeness of the descriptions. He wrote up all his own observations, and included with them, the observations of all his predecessors in a series of books, which remained the standard in anatomy for 1500 years. ⁵⁶ Though this time, we as a species, following the teachings of Aristotle, observed Nature first hand, with our own eyes, to get an understanding of questions such as: "What is the nature of life? Who are we? What is the nature of the world? What is our relationship to the Universe?"

With the rise of Christianity, there were some leaders, including Tertullian (ca. 155-ca. 230) who expressed the opinion more often than not that answers to these questions could only come from church authority and not though scientific inquiry. By contrast, Augustine of Hippo (354-430), who later became a Saint in the Catholic Church, searched for answers about the nature of life though inquiry based upon faith and reason. Augustine appreciated natural philosophical studies and argued that reason, which is based upon the "Book of Nature" took precedence over faith, which is based on the Bible when it came to understanding the nature and creation of the material world. This acceptance would prevent the unbelievers from considering the believers to be fools.⁵⁷ Augustine's deep thinking was unappreciated and as a rule, the citizens of the Roman Empire were not interested in any process of discovery, researching and questioning the nature of the world, but were content with accepting without question the answers already derived by the Ancients, particularly Plato, Aristotle, Euclid, Ptolemy and Galen. The learned citizens of the Latin West read commentaries (i.e., reviews) on the Ancients written by scholars such as Theon of Smyrna, Proclus, Simplicius and Philoponus; and the encyclopedias written by Celsus, Cato, Varro and Pliny.⁵⁸ The encyclopedias contained the answers, but did not record how the answers were obtained. The readers accepted the words of the authorities without question.

The fall of the Roman Empire did not bring about a revival of independent thinking and learning. During the Middle Ages, with a few exceptions, ^{59,60} it seems that as a species, we were not interested in the enterprise of discovery, nor were we fascinated with the discovery of the unknown. In the Monasteries and the newly founded Cathedral Schools, we asked no new questions. We were content to know the answers given by the authorities of the time, and scholars merely transcribed the Bible, and other manuscripts written by the ancient authorities. All was not dark however. While Europe was suffocating in an intellectual stupor, the Arab world was resplendent with scientific curiosity and achievement. Arab scholars translated Greek works and expanded upon them with experiments. Thus, the years 900–1100 were to become the golden age of mathematics, medicine and technology for Islam.⁶¹

In the 12th and 13th centuries AD, a new interest in learning arose in Europeans after the crusaders conquered some of the Arabic-speaking peoples, and Arabic translations of the original Greek texts of Aristotle and others became available. During this time, the first great universities of Europe (Paris, Bologna, Oxford and Cambridge) became established.⁶² However, education was still under the attentive supervision of the Church, and all universities in Christian countries had to obtain the Pope's sanction for their continued existence.⁶³ With the reintroduction of Greek science, new problems emerged. People were still interested in the teachings of authority; however, now there were two authorities: Aristotle and the Bible. Moreover, the natural philosophical teachings of Aristotle the pagan appeared to

contradict the teachings of the Bible. In 1210, 1215 and 1231, there were bans and attempts to ban Aristotle's books in the University of Paris. Scholars, with few exceptions, were *not* interested in resolving the two opposing theses, and consequently believed in the "double truth". That is, there was no relationship between the truths of natural philosophy and the truths of theology. Natural philosophy pursued by Catholic scholars, including William of Conches was just an academic subject, with no obvious relationship to reality.

Thomas Aquinas, a Dominican monk, made Aristotle safe for the church by reinterpreting Aristotle's natural philosophic writings in terms of Christianity. For example, the unmoved mover (or uncaused causer) in Aristotle's Universe, was the God of the Bible. Aquinas, who was soon to be sainted, concluded that there was only one real truth. Thus the truth obtained by reason must coincide with the truth obtained by revelation in the Scriptures and there must be a harmony between natural philosophy and theology in the discovery of the one self-consistent truth. Aquinas, like Augustine, believed that the Word of God as presented in the Scriptures, while not literally true, was ultimately true, and he accepted enough natural philosophy in his exegesis of the Scriptures so that unbelievers would not scorn the Scriptures.

While Aristotle and the Bible were taught in the 13th century, natural philosophy became less than a handmaiden to theology. Instead of encouraging questioners to find the ultimate truths though the synthesis of opposites, the church began to suppress the type of questioning that did not support the current dogma. The bishops that oversaw certain major universities put out lists in 1270 and 1277 condemning ideas of natural philosophy which were inconsistent with the theological teachings. 65,66

Religion at this time, instead of providing an environment where questions about the nature of the world could be asked, decided it had the answers, and it became blasphemous to ask the questions. Natural philosophy, although still studied, was studied to a large extent by disputation and argument, and not by making new observations and gathering new data. In medical schools, physicians studied the Galenic texts and did not even perform dissections in order to get first hand knowledge of the body as Galen had done. They just observed the dissections that occurred once or twice a year in public theaters. In fact, the physician in charge of the public dissection read from Galen (in Latin), but did not even dirty his hands at the dissection. This was the job of the barber-surgeon (i.e., technician). The Church was not monolithic in its suppression of discovery and questioning. Indeed, at a time when the physicians and barber-surgeons were protecting the tradition of purging and bleeding to fight malaria, some members of the church, particularly Cardinal Juan de Lugo encouraged experimentation aimed at curing the deadly malaria with an extract from the Peruvian fever-bark tree that later came to be known as quinine.⁶⁷

In the 16th century, the Humanists, including Vesalius, began to stress the importance of doing things as well as the ancients, or even better.⁶⁸ The Humanists emulated the questioning nature of the ancients, not their authority. This meant that a physician should know the ancient texts, be able to perform dissections himself, and do it even better than Galen himself in order to further our knowledge. This tradition was carried on, and extended by Realdo Columbo, Fabricius⁶⁹ and William Harvey. They looked at anatomy as Aristotle did. They asked questions, they found new answers, and asked more

questions. Indeed the spirit of discovery, expressed in Aristotle, reappeared in the Humanists. Feeling the connection between Aristotle and himself, Harvey⁷⁰ entitled one of his books: "On the Generation of Animals"; the same title used by Aristotle.

The new freedom of discovery exercised by the Humanists was not felt by all. Johannes van Helmont, another physician, was called in front of the Spanish Inquisition in 1625 because of his ideas about the importance of chemistry in understanding medicine. Chemistry was considered a diabolical art, and van Helmont was placed under house arrest by the Inquisition until two years before his death. Similarly, the Roman Inquisition was not too fond of an Italian natural philosopher and mathematician named Galileo Galilei. 71,72 He had the audacity to believe that the Earth was not the center of the Universe. Problematic indeed, for if the Earth went around the Sun, then not every word of the Bible would be correct. Joshua (10:12-13) says that Joshua asked God to make the Sun stand still so he could continue his fight. Thus the Sun must go around the Earth and not vice versa. Like van Helmont, Galileo was placed under house arrest in 1633. He might be pleased to learn that the Catholic Church reversed its stand on his works in 1993.

Perhaps the condemnations inspired those interested in knowing the nature of the world to turn to experiment. Aristotle had always made a distinction between Art and Nature. According to Aristotle, they had different final causes: Art resulted from human causes; whereas Nature unfolded spontaneously due to natural causes. Thus many people considered that an experiment could never be used to understand Nature because an experiment was set up with human ends in mind, not natural ends. Consequently, the conclusions drawn from experiments designed to study Nature under artificial conditions were not then considered to be as threatening to the religious authorities as the conclusion drawn from the direct observation of natural phenomena. At this time, Francis Bacon published his version of the scientific method, which specified a method for observing Nature and accentuated the importance of building limited generalizations based upon sound observational data.^{73,74}

René Descartes,⁷⁵ John Locke⁷⁶ and David Hume⁷⁷ emphasized the importance of analysis, sensation and experience, respectively for understanding the world. Following the introduction of experimental philosophy, science became extremely successful in describing and explaining the world.⁷⁸⁻⁸¹ Through the 17th and 18th centuries, work by model scientists combined experimental methods and natural philosophy to change our view of the world around us and our view of life itself. Indeed, like Augustine and Thomas Aquinas, these model scientists, including Kepler, Copernicus, Galileo, Robert Boyle, Robert Hooke and Isaac Newton questioned nature in order to understand the works of God.

While the Catholic Church must take responsibility for discouraging the questioning of authorities and Nature though the banning of books in the 13th century and the Inquisition in the 17th century, the relationship between science and religion in general has been mutually invigorating much like the relationship expounded by Augustine when he said, "I believe so that I may understand" and "I understand so I may believe." The idea that the Church was intolerant of science throughout history and that the free questioning of nature is the province of universities was inaccurately⁸² and unfairly⁸³ portrayed in the 19th century by John William Draper⁸⁴ and Andrew Dickson White.

The power of scientific skepticism of the 19th century was evident both scientifically and technologically through the growth of the industrial revolution. Perhaps just as it seemed that science had explained almost everything from the unity of energy to the unity of organisms by such all-encompassing theories like the theory of conservation of energy,^{87,88} the cell theory,^{89,90} and the theory of evolution by natural selection,⁹¹ it was shown by Max Planck, Niels Bohr, Albert Einstein, Werner Heisenberg, Erwin Schrödinger, Louis de Broglie and others, that some of the "classic" theories used to explain the nature of the world were limited. ⁹²⁻¹⁰⁵ As a scientific community, we are usually proud of these revolutionary model scientists for having the courage to question the widely accepted theories; and having the experimental and/or mathematical means to show that their new theories were better approximations of the truth than the previous theories.

The 20th century saw an enormous growth in biological knowledge. To a large extent we know how life continues from generation to generation, and how the DNA in the nucleus is replicated in order to fulfill this function. 106 We know much about how the instructions encoded by the DNA in the nucleus are transferred to the cytoplasm, and brought to fruition by the action of proteins. 107-109 We have developed and subsequently overturned the "Central Dogma", 110 demonstrating that this dogma, like all others has its limitations. We know much about the cellular localization of enzymes, and the function of organelles. 111-114 We know much about how the chloroplast uses the energy of sunlight to convert inorganic molecules like CO₂, H₂O and NO₂ into sugars and amino acids that are used to form the molecules necessary for life. 115,116 We know much about how the mitochondrion converts the energy inherent in carbohydrate molecules into ATP,¹¹⁷ the hydrolysis of which provides the energy for almost every cellular reaction. 118 We know much about how the plasma membrane regulates what enters and leaves the cell so that the cell can concentrate needed molecules, expel others, and maintain a homeostasis in an ever-changing environment. 119 We know much about how the cell perceives external stimuli and converts them into an adaptive response. We know to a large extent how specialized cells like muscle cells, neurons, mesophyll cells and root hairs function so that a whole organism can live. 120,121 We know much about how individuals and species adapt to, and cooperate and compete within a community. 122,123 We even know something about the origin of life and the mechanism of evolution. 124,125 To a large extent, if not exclusively, these discoveries were made by independent model scientists, who used the best systems and techniques to answer a specific question about the nature of life.

How many of these discoveries would have been made if the model scientists were restricted by authorities to work on a few "model systems", to use a limited number of techniques or to do research that would yield short-term economic profits? When we think of this question, we wonder why so many job descriptions specify that the successful applicant will use certain techniques and "model organisms". How can we change the focus from model organisms accepted *ex cathedra* to model scientists? We suggest that each of us, individually, choose our own model scientists and find their books and papers and read their own words. Then we should emulate their spirit of discovery and their ability to discover new facts, make new generalizations, and come up with new theories on the nature of life. We should not just imitate their use of a certain technique or

organism.⁴ Emulating their spirit of discovery takes a great deal of personal courage.

In the new millennium, money has become the highest pontifical authority in biology. Consequently, the study of biology in universities is changing, and change does not always equate with progress. Ironically, biology has become "genomics", a name intentionally created to minimize any academic associations. 126,127 Research in the field of genomics or any other of the super-funded—omics is capable of garnering enormous sums of money to universities through indirect costs, patent royalties and licensing agreements and this is of great interest to Deans, Provosts and Presidents. At many universities, pecuniary interests have caused the administration to usurp the traditional rights and responsibilities of the faculty to determine the direction of their departments. Since the administrators may have a tendency to equate science that brings in vast sums of money with excellent science, we believe that the future direction of science is in danger of being influenced more by pecuniary instincts than the instincts of workmanship and curiosity. 128-137 The influence of pecuniary interests will reduce the "degrees of freedom" necessary to discover new phenomena. 138 Consistent with the cycles of history, during this same period (September 15, 1998), Pope John Paul II came out with an Encyclical Letter stating the primacy of questioning. He wrote, "In effect, every philosophical system, while it should always be respected in its wholeness, without any instrumentalization, must still recognize the primacy of philosophical *enquiry*, from which it stems and which it ought loyally to serve."

The transference of power from the scientific questioners to the administration in determining the direction of science sends a chilling message to all faculty members. That is, the first question that must be asked when pursuing biological research will no longer be, "How can we better understand the biological basis of life?" but "Will the proposed research bring in a substantial amount of money to the university through indirect costs, patent royalties and licensing agreements?" We are in jeopardy of returning to the medieval ways of merely copying, transcribing or perhaps embellishing existing theories, albeit at great expense using high cost state-of-the-art methods. A preoccupation with fundable, Apollonian science will send a message to faculty and by example to our students—not to be independent and wise thinkers worthy of our specific epithet, Homo sapiens, but to work on projects whose results are certain enough to garner large monetary rewards. After all, according to Albert Szent-Györgyi, "A discovery must be, by definition, at variance with existing knowledge."22 And who in their right mind is going to throw large sums of money at something that is at variance with existing knowledge? The scientific Prometheans of the 17th-20th centuries stunned their contemporaries with new insights into the workings of the natural world. Ironically, contemporary science is in danger of creating a cheerless variation of the Promethean myth: 139 we, the beneficiaries of the knowledge of Nature, wrested for us by the scientific Prometheans, are binding ourselves to the rocks, by becoming sellers, rather than stealers of the unknown fire. To paraphrase Szent-Györgyi, the current policy may do its greatest harm by making faculty and students avoid problems that do not have short-term monetary benefits.²³ We will be, according to Chargaff, a faculty of "lost souls teaching the young to lose theirs." ¹⁴⁰

Using science for the pursuit of individual or institutional wealth is having an unintended consequence for science, particularly biology.

As the recent Vioxx lawsuits show, academics are selling their names and the integrity of their institutions to promote products. 135,141 In discussing David Michael's new book, "Doubt is Their Product: How Industry's Assault on Science Threatens Your Health", Sharon Begley wrote in an article in Newsweek, "This book will shock anyone who still believes that 'science' and 'integrity' are soulmates." 142 The news is reporting to us that science is now in danger of being assaulted from within.

Can this grim outcome be avoided? Probably. But only with a reversion of our ideal of good science to "that which reveals the underlying laws of Nature" from "that which attracts the most funding." We must recognize the distinction between, and the value of both, Dionysian and Apollonian science,²² while acknowledging that it is the Dionysian, the unfundable, science that will most likely result in advances in our understanding of Nature.

I Think

I.

I think that I will never see An Arabidopsis as beautiful as a pea.

I think that I will not discern An Arabidopsis as beautiful as a fern.

I think I would be at a loss
To find an Arabidopsis as beautiful as a moss.

I think it will not come to pass
That I will see an Arabidopsis as beautiful as a grass.

I think that I will rarely gander At an Arabidopsis as beautiful as a jacaranda.

I think that I will seldom notice An Arabidopsis as beautiful as a lotus.

I think that I will never find.

An Arabidopsis as beautiful as a plant of ANY KIND!!!!!

II.

I think I'll never get a grant If I work on any other plant!

III.

It's now fifteen years later and things have changed But funding for science is still deranged.

I think that we would all be fools to study plants—not biofuels.

- -Randy Wayne
- -Mark Staves

(From Poetry of the Vegetable World)

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Note

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2008; Vol. 1 Issue 1

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